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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. |
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| EXAMINER | |
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| SCHWADRON, R | |
| **ART UNIT** | **PAPER NUMBER** |
| 1644 | 22 |

**DATE MAILED:** 04/24/01

**Please find below and/or attached an Office communication concerning this application or proceeding.**

**Commissioner of Patents and Trademarks**

PTO-90C (Rev.11/00)

1- File Copy

# Office Action Summary

| Application No. | Applicant(s) | |
|---|---|---|
| 09/127411 | Gruenberg | |
| **Examiner** | **Group Art Unit** | |
| Ron Schwadron, Ph.D. | 1644 | 22 |

*—The MAILING DATE of this communication appears on the cover sheet beneath the correspondence address—*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, such period shall, by default, expire SIX (6) MONTHS from the mailing date of this communication .
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).

**Status**

☐ Responsive to communication(s) filed on 2/9/2001 and 11/8/2001.

☒ This action is **FINAL.**

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 1 1; 453 O.G. 213.

**Disposition of Claims**

☒ Claim(s) 36-40, 154-167 is/are pending in the application.

Of the above claim(s) 36, 38, 40, 154-157, 158, 162, 163, 164, 166 is/are withdrawn from consideration.

☐ Claim(s) _____ is/are allowed.

☒ Claim(s) 37, 39, 159-161, 165, 167 is/are rejected.

☐ Claim(s) _____ is/are objected to.

☐ Claim(s) _____ are subject to restriction or election requirement.

**Application Papers**

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The proposed drawing correction, filed on _____ is ☐ approved ☐ disapproved.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☐ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

**Priority under 35 U.S.C. § 119 (a)-(d)**

☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 11 9(a)-(d).

☐ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been

☐ received.

☐ received in Application No. (Series Code/Serial Number) _____.

☐ received in this national stage application from the International Bureau (PCT Rule 1 7.2(a)).

*Certified copies not received: _____.

**Attachment(s)**

☒ Information Disclosure Statement(s), PTO-1449, Paper No(s). _____

☐ Interview Summary, PTO-413

☐ Notice of Reference(s) Cited, PTO-892

☐ Notice of Informal Patent Application, PTO-152

☐ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Other _____

**Office Action Summary**

1. Claims 37,39,159-161,165,167 are under consideration. Claims 159-161,165,167 are newly added. Claims 158,162-164,166 are withdrawn from consideration in that they depend from nonelected species as per the previous Office Actions.

2. Applicants comments regarding the species election are addressed in paragraph 1 of the Office Action mailed 5/8/2000.

## RESPONSE TO APPLICANTS ARGUMENTS

3. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

4. Claims 37,39,159-161,165,167 stand rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Applicants arguments have been considered and deemed not persuasive.

There is no support in the specification for the recitation of "isolating mononuclear cells" in claim 37 (said language is actually recited in nonelected claim 36 upon which claim 37 depends). The original claims disclose the claimed method wherein the claim recites "isolating CD4+ mononuclear cells", but not the claimed invention which recites "isolating mononuclear cells". There is no disclosure in the specification as originally filed of the scope of the claimed invention (eg. it constitutes new matter).

Regarding applicants comments, the specification, pages 13,14,28 or 29 do not refer to the claimed method (eg. expansion of virally purged Th1 cells). The original claims disclose the

claimed method wherein the claim recites "isolating CD4+ mononuclear cells", but not the claimed invention which recites "isolating mononuclear cells". There are numerous different methods disclosed in the specification which use different steps. Examples 1 and 2 in the specification are not drawn to the scope of the claimed invention (eg. they refer to methods involving normal cells, not expansion of virally purged Th1 cells).

5. Claims 37,39,159-161,165,167 stand rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Applicants arguments have been considered and deemed not persuasive.

There is no support in the specification for the recitation of "mitogenic antibodies" in claim 37 (said language is actually recited in nonelected claim 36 upon which claim 37 depends). The specification and original claims disclose use of "mitogenic monoclonal antibodies", but not use of "mitogenic antibodies". Said term encompasses the use of antibodies other than monoclonal antibodies (eg. polyclonal antibodies, monospecific polyclonal antibodies, recombinant antibodies, etc), wherein the use of such antibodies in the claimed method is not disclosed in the specification a originally filed. There is no disclosure in the specification as originally filed of the scope of the claimed invention (eg. it constitutes new matter).

6. Claims 37 and 39 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 37 and 39 are indefinite in that they depend on nonelected claim 36.

Applicants comments have been noted.

7. Regarding priority for the claimed inventions with regards to the application of prior art, the claimed inventions are not disclosed in parent application provisional application 60/044693 (the application formerly known as 08/506668), and therefore priority with regards to the application of prior art is taken as the filing date of parent application 08/700565 to which applicant claims priority.

Regarding applicants comments, the only disclosure of a method for producing virally

purged Th1 cells in parent application 60044693 is Example 2. Said example is not of the scope of the claimed invention (eg. it is limited to use of a particular method for purifying starting cells, wherein said cells are stimulated with two particular antibodies (antiCD3 and antiCD28) and interferon-gamma). Applicant has referred to various parts of the parent application that refer to methods other than the claimed method. Applicant appears to be arguing that the claimed method is obvious based on other methods disclosed in the specification. However, obviousness is not the appropriate standard with regards to issues of written description. The CAFC stated in Lockwood v. American Airlines Inc., 41 USPQ2d 1961 (Fed. Cir. 1997) that:

*3. Patentability/Validity -- Specification -- Written description (§ 115.1103)*
*Patent's entitlement to earlier filing date extends only to that which is disclosed in prior application, and does not extend to subject matter which is not disclosed, but would be obvious over what is expressly disclosed; one shows that one is "in possession" of invention of patent by describing invention, with all its claimed limitations, not that which makes it obvious, and although prior application need not describe claimed subject matter in exactly same terms used in claims, prior specification must contain equivalent description of claimed subject matter, and description which renders obvious invention for which earlier filing date is sought is not sufficient.*

The CAFC also stated in Lockwood v. American Airlines Inc., 41 USPQ2d 1961 (Fed. Cir. 1977) that:

*The invention is, for purposes of the 'written description' inquiry, whatever is now claimed .") (emphasis in original). One does that by such descriptive means as words, structures, figures, diagrams, formulas, etc., that fully set forth the claimed invention. Although the exact terms need not be used in haec verba , see Eiselstein v. Frank , 52 F.3d 1035, 1038, 34 USPQ2d 1467, 1470 (Fed. Cir. 1995) (" [T]he prior application need not describe the claimed subject matter in exactly the same terms as used in the claims.. . ."), the specification must contain an equivalent description of the claimed subject matter. A description which renders obvious the invention for which an earlier filing date is sought is not sufficient.*

8. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person

having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

9. Claims 37,39,159-161 are rejected under 35 U.S.C. § 103 as being unpatentable over O'Garra et al. in view of June et al. (WO 94/29436) or June et al. (US Patent 5,858,358) and Carew (US Patent 5,123,901) and Nabel.

O'Garra et al. teach that Th1 can be produced by treating CD4+ cells with IL-12 (see page 460) or interferon γ (see Figure 1). O'Garra et al. do not teach the claimed method of producing virally purged Th1 cells with the numbers of cells recited in the claims. June et al. (WO 94/29436)(Figures 1 and 2, pages 4-35) or June et al. (US Patent 5,858,358)(Figures 1 and 2, columns 4-32) both teach methods of expanding T cells to clinically relevant numbers without using exogenous growth factors (see abstract). Figures 1 and 2 of said publications show expansion of T cells to greater than $10^{10}$ cells. Nabel teaches that T cell activation results in production of HIV virus in latently infected T cells (see Abstract). Carew teaches that HIV positive T cells can be removed from blood or a fluid containing said infected cells by treatment with immunoreactive beads coated with a reagent that binds HIV (see Abstract and column 2, last paragraph). A routineer would have prepared said cells at any desired concentration. It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to have created the claimed invention because O'Garra et al. teach that Th1 can be produced by treating CD4+ cells with IL-12 or interferon γ while June et al. (WO 94/29436) or June et al. (US Patent 5,858,358) both teach methods of expanding T cells to clinically relevant numbers and Carew teaches that HIV positive T cells can be removed from blood or a fluid containing said infected cells by treatment with immunoreactive beads coated with a reagent that binds HIV. One of ordinary skill in the art would have been motivated to do the aforementioned because June et al. teach a variety of uses for expanded T cell subsets and because Carew teaches that HIV infected T cells should be removed from blood products that are administered to humans (see abstract).

10. Claims 37,39,159-161 are rejected under 35 U.S.C. § 103 as being unpatentable over Seder al. in view of June et al. (WO 94/29436) or June et al. (US Patent 5,858,358).

Seder et al. teach that Th1 (eg. interferon γ producing cells derived from CD4+ T cells) can be produced by treating CD4+ cells with IL-12 (see abstract) or interferon γ (see page

10190, second column, last paragraph, first sentence). Seder et al. do not teach the claimed method of producing virally purged Th1 cells with the numbers of cells recited in the claims. June et al. (WO 94/29436)(Figures 1 and 2, pages 4-35) or June et al. (US Patent 5,858,358)(Figures 1 and 2, columns 4-32) both teach methods of expanding T cells to clinically relevant numbers without using exogenous growth factors (see abstract). Figures 1 and 2 of said publications show expansion of T cells to greater than $10^{10}$ cells. June et al. teach a variety of uses for said expanded T cell compositions (see column 18-20 or pages 21-23). Nabel teaches that T cell activation results in production of HIV virus in latently infected T cells (see Abstract). Carew teaches that HIV positive T cells can be removed from blood or a fluid containing said infected cells by treatment with immunoreactive beads coated with a reagent that binds HIV (see Abstract and column 2, last paragraph). A routineer would have prepared said cells at any desired concentration. It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to have created the claimed invention because Seder et al. teach that Th1 can be produced by treating CD4+ cells with IL-12 or interferon $\gamma$, while June et al. (WO 94/29436) or June et al. (US Patent 5,858,358) both teach methods of expanding T cells to clinically relevant numbers and Carew teaches that HIV positive T cells can be removed from blood or a fluid containing said infected cells by treatment with immunoreactive beads coated with a reagent that binds HIV. One of ordinary skill in the art would have been motivated to do the aforementioned because June et al. teach a variety of uses for expanded T cell subsets and because Carew teaches that HIV infected T cells should be removed from blood products that are administered to humans (see abstract).

11. Claims 165 and 167 are rejected under 35 U.S.C. 103(a) as being unpatentable over O'Garra et al. in view of June et al. (WO 94/29436) or June et al. (US Patent 5,858,358) and Carew (US Patent 5,123,901) and Nabel as applied to claims 37,39,159-161 above, and further in view of Cracauer et al. (US Patent 4,804,628).

The previous rejection renders obvious the claimed method except for use of a hollow fiber reactor. Cracauer et al. teach hollow fiber bioreactors and that the use of such hollow fiber bioreactors for efficiently growing larger numbers of cells in vitro (see columns 1-3). It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to have created the claimed invention because the previous rejection render obvious the claimed method except for the use of a hollow fiber bioreactor and Cracauer et al. teach hollow

fiber bioreactors and that the use of such hollow fiber bioreactors for efficiently growing larger numbers of cells in vitro. One of ordinary skill in the art would have been motivated to do the aforementioned because Cracauer et al. teach that "hollow fiber culture devices have been proven to be ideal for the maintenance of many types of cells at high densities in culture."(column 1).

12. Claims 165 and 167 are rejected under 35 U.S.C. 103(a) as being unpatentable over Seder et al. in view of June et al. (WO 94/29436) or June et al. (US Patent 5,858,358) and Carew (US Patent 5,123,901) and Nabel as applied to claims 37,39,159-161 above, and further in view of Cracauer et al. (US Patent 4,804,628).

The previous rejection renders obvious the claimed method except for use of a hollow fiber reactor. Cracauer et al. teach hollow fiber bioreactors and that the use of such hollow fiber bioreactors for efficiently growing larger numbers of cells in vitro (see columns 1-3). It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to have created the claimed invention because the previous rejection render obvious the claimed method except for the use of a hollow fiber bioreactor and Cracauer et al. teach hollow fiber bioreactors and that the use of such hollow fiber bioreactors for efficiently growing larger numbers of cells in vitro. One of ordinary skill in the art would have been motivated to do the aforementioned because Cracauer et al. teach that "hollow fiber culture devices have been proven to be ideal for the maintenance of many types of cells at high densities in culture."(column 1).

13. No claim is allowed.

14. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this

final action.

15. Papers related to this application may be submitted to Group 1600 by facsimile transmission. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). Papers should be faxed to Group 1600 at (703) 308-4242.

16. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Dr. Ron Schwadron whose telephone number is (703) 308-4680. The examiner can normally be reached Monday through Thursday from 7:30 to 6:00. A message may be left on the examiners voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ms. Christina Chan can be reached on (703) 308-3973. Any inquiry of a general nature or relating to the status of this application should be directed to the Group 1600 receptionist whose telephone number is (703) 308-0196.

RONALD B. SCHWADRON
PRIMARY EXAMINER
GROUP 1600

Ron Schwadron, Ph.D.
Primary Examiner
Art Unit 1644